

## REMARKS

Claims 1, 4-6, 10, 16-18 and 20-32 are pending and under consideration.

### Rejection under 35 U.S.C. § 103(a)

Claims 1, 4-6, 10, 16-18 and 20-32 are rejected under 35 U.S.C. § 103(a), as, allegedly, obvious over International Patent Publication No. WO 92/15285 by Lentz *et al.* ("Lentz"). According to the Examiner, given the teachings of Lentz, the claimed invention is obvious in view of the overlapping ranges of the process temperatures of the prior art and the present invention. Applicants respectfully disagree with the Examiner.

Preliminarily, Applicants, in order not to burden the record, hereby incorporate by reference the remarks made in the last response with regard to the teachings of Lentz and present the following additional argument and evidence.

Applicants point out that the Examiner's contention that there is an overlap of temperatures between the extrusion method of the present invention and the method disclosed in Lentz is incorrect. Applicants invite the Examiner's attention to the accompanying Declaration of Dr. Hubert Rein under 37 C.F.R. § 1.132 ("the Rein Declaration"). In particular, Dr. Rein, a co-inventor of the present invention, in Paragraph 6 states:

Importantly, the teaching of Lentz regarding the temperature range of 80°C to 240°C for processing does not mean that the processing can take place at any temperature between 80°C to 240°C but rather means that the entire process occurs at temperatures encompassing 80°C to 240°C, never just at 80°C or 130°C or 240°C. This is an important distinction as, contrary to the Examiner's assertion, there are no overlapping temperatures between the two processes. One skilled in the art of extrusion would clearly understand that Lentz is giving the range of the temperatures of the extruder, which temperatures differ at different locations of the extruder. Lentz specifically teaches on page 28, lines 17-19 that the extruder barrel temperature profile was 80°C - 160°C - 240°C (for feed, screw and die, respectively). One skilled in the art would understand that the temperature of the extruder orifice (die) is 240°C. This is an important distinction between the teachings of Lentz and the presently claimed invention, where the orifice of the extruder is below 100°C, which also means that all other parts of the extruder are below 100°C.

Further, Dr. Rein states in Paragraph 7:

The only passage in Lentz that concerns co-extrusion of a pharmaceutically active agent and a starch is on page 17, line 37 to page 18, line 1. However, there are absolutely no details in the Lentz specification to teach one skilled in the art how such a co-extrusion can be carried out, unless the co-extrusion is carried out by the same methodology as Lentz uses to extruded the starch alone. Example 18 in Lentz, however, does provide details for a method of

co-extrusion. However, Example 18 teaches co-extrusion of not starch but molecularly dispersed starch (which was previously extruded starch) with an active agent (clotrimazole) and talc. Further, as explicitly stated by Lentz, the resulting co-extruded product is a foamed, rubbery product, which is not a controlled release matrix. The pending claims require that the matrix produced by the method be a vitrified controlled release matrix, *i.e.*, glassy. A foamed, rubbery product is not a glassy vitrified product.

Thus, not only does Lentz not teach or suggest any overlapping temperatures for the extrusion process, in the only co-extrusion example set forth in Lentz, the result was a foamy, rubbery product that is not a controlled-release product.

A rejection for obviousness is improper when there is nothing in the cited prior art reference suggests the desirability of the claimed subject matter. For a rejection of claimed subject matter as obvious (1) the prior art must have suggested to those of ordinary skill in the art that they should make the claimed composition or device or use the claimed method, as the case may be; and (2) the prior art must have revealed that in so doing, those of ordinary skill would have had a reasonable expectation of success. *In re Vaeck*, 947 F.2d 488, 20 USPQ2d 1438 (Fed. Cir. 1991); *In re Dow Chemical Co.*, 837 F.2d 469, 5 USPQ2d 1529 (Fed. Cir. 1988). The suggestion of the claimed invention must be in the prior art, not in the disclosure of the claimed invention. *In re Dow Chemical Co.*, 837 F.2d 469, 5 USPQ2d 1529 (Fed. Cir. 1988). In the present case, the presently claimed methods are directed to the production of a controlled release matrix by co-extrusion of a dry mixture of a starch and an active agent where the temperature at the orifice of the extruder during the extrusion process is below 100°C under normal pressure. Lentz does not teach or suggest a modification of its disclosed method requiring that the temperature at the orifice of the extruder (as well as all other parts of the extruder) during the extrusion process be below 100°C under normal pressure. Lentz does not teach or suggest that the temperature be kept under 100°C, and the only time Lentz actually co-extruded an active agent with its molecularly dispersed starch, no controlled release product was achieved. Lentz does not and cannot render the claimed invention obvious.

Moreover, Applicants have now provided experimental evidence comparing the process of the present invention, where the temperature of the extruder orifice is below 100°C, with the process taught by Lentz, where the temperature of the extruder orifice is 240°C. The Examiner's attention is invited to the Rein Declaration at Paragraphs 8 to 12 where Dr. Rein sets forth experiments that were performed or supervised and directed by him, and their results demonstrating that using the process of Lentz (over 100°C) only popped (foamed) products are produced, whereas using the process of the present invention (under 100°C) a vitrified product is

produced, which product is a controlled-release product. Thus, this experimental evidence overwhelmingly shows that two different products are produced using the two different methods.

In view of the foregoing, Applicants respectfully request that the rejection under Section 103(a) in view of Lentz be withdrawn.

**CONCLUSION**

Applicants respectfully request that the above-made remarks of the present response be entered and made of record in the file history present application. Applicants submit that the presently pending claims meet all requirements for patentability and respectfully request allowance and action for issuance.

Applicants request that the Examiner call the undersigned at (212) 326-3921 if any questions or issues remain.

Respectfully submitted,

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Enclosures